REMARKS

Claims 42-50 are pending in the application and were subject to examination. Claims 42-50 were rejected under 35 U.S.C. § 112, first paragraph, with the Examiner stating that these claims fail to comply with the written description requirement. This rejection is respectfully traversed.

As was noted by the Examiner, claims 42-50 specify methods of inhibiting amyloid β peptide polymerization by administration of therapeutically effective amounts of particular compounds, including compounds comprising the sequence VHHQKLVFFA or HHQKLVFFAE. As a basis for the rejection, the Examiner states that the "specification, at best, discloses that such peptides bind Aβ (see Fig. 2A and Example 1); specification does not disclose that said peptides inhibit polymerization of amyloid peptide either in vitro or in vivo. The only demonstration of inhibit polymerization of amyloid peptide is provided for peptide $AcKLVFFNH_2$, in Example 3, pages 12-13. This is a new matter rejection" (Office Action, paragraph spanning pages 2 and 3).

In response, Applicants submit that claims 42-50 do not add new matter, as the use of peptides, such as those specified in these claims, in methods of inhibiting polymerization of amyloid β peptide is clearly described in the application. Further, as is stated in M.P.E.P. § 2163.07, "amendments to an application which are supported in the original description are NOT new matter." (Emphasis in original.)

Examples of support for claims 42-50, with respect to the use of the peptides of these claims in the inhibition of amyloid β peptide polymerization (both in vitro and in vivo), is summarized below.

Figures 2A and 2B

These figures show the binding of different amyloid β peptides to Aβ 1-40. For example, results obtained with peptides 12-21 and 13-22 (as specified in the present claims) are provided in Figure 2A. As is made clear in the passages of the specification set forth below, binding of peptides to Aβ 1-40 correlates with the inhibition of Aβ polymerization.

Page 1, lines 10-15:

"The present invention relates to compounds, which are of special interest by their ability to bind to the KLVFF-sequence in the peptide amyloid β and to **inhibit polymerization** of the amyloid β peptide." (Emphasis added.)

Page 3, lines 20-37:

"It was assumed that ligands which bind to recognition sequences would be capable of **inhibiting Aβ polymerization** and possibly also dissolve preformed Aβ polymers *in situ*. The strategy in finding such Aβ ligands was to identify critical binding regions in Aβ and, based on their sequences, develop a compound capable of blocking the Aβ-Aβ binding.

According to the invention, it was hypothesized that compounds capable of binding to regions in the Aβ-molecule critical for its polymerization might **inhibit amyloid fibril formation**, as described in more detail below.

According to the invention, it has now been found that **the Lys-Leu-Val-Phe-Phe (KLVFF) sequence in Aβ is necessary for polymerization to occur. Peptides incorporating this sequence bind to Aβ and are capable of blocking the fibril formation of Aβ-1-40 and**

are therefore potentially useful as drugs." (Emphasis added.)

Page 4, lines 9-15:

"Thus, it was concluded that the Lys-Leu-Val-Phe-Phe (16-20) motif serves as a structural basis for the development of peptide and non-peptide agents aimed at **inhibiting amyloidogenesis *in vivo***. This is a novel finding and the compounds are of utmost interest as being useful as drugs for Alzheimer's disease." (Emphasis added.)

Page 6, lines 1-3:

"In a preferred embodiment of the present invention, the compound exhibits an ability to **inhibit polymerization of amyloid β** peptide." (Emphasis added.)

Page 8, lines 12-24:

"Also claimed is the use of a compound, preferably of the formula (I) or (II), which is able to bind to the KLVFF-sequence in amyloid β peptide and which has the ability to **inhibit polymerization of amyloid β** peptide, for the manufacture of a medicament for the treatment or prevention of amyloidosis, especially in the treatment or prevention of Alzheimer's disease associated with amyloidosis, for the treatment or prevention of demens in patients with Down's syndrome, for the treatment or prevention of Hereditary cerebral hemorrhage with amyloidosis (Dutch type) or for the prevention of fibril formation of human amyloid protein." (Emphasis added.)

Page 14, lines 22-24:

"Like KLVFF, the D-amino acid ligands were found not only to bind to Aβ but also to **inhibit amyloid fibril formation**." (Emphasis added.)

Page 14, lines 27-33:

"The results further indicate that KLVFF will be useful in the identification of small organic molecules (e.g. by screening of substance libraries) with the ability to bind to Aβ in this relevant region and **inhibit amyloid fibril formation** (candidate drugs for the treatment of Alzheimer disease and other related amyloidoses)." (Emphasis added.)

Page 15, lines 31-36:

"Hence, a molecule capable of binding to a site in the Aβ molecule that is critical for **fibril formation** with an affinity higher that native Aβ should have reasonable chances to inhibit amyloid growth and maybe also specifically dissolve amyloid fibrils." (Emphasis added.)

Page 16, lines 1-6:

"In conclusion, we have identified an Aβ sequence, KLVFF, which is required for **amyloid fibril formation**. The KLVFF peptide may serve as a model substance for the synthesis of non-peptide Aβ-ligands that **interfere with the polymerization of Aβ** molecules." (Emphasis added.)

Page 16, lines 14-22:

"It was also demonstrated that short peptides incorporating Aβ-16-20 can function as ligands that bind to Aβ and **inhibit the formation of amyloid fibrils**. Since these peptide ligands are relatively small, they are amenable for identification of other organic molecules with similar functional properties. Non-peptide homologues of KLVFF should be useful as pharmacological drugs for the treatment of Alzheimer's disease in the future." (Emphasis added.)

In view of the above, the rejection for lack of adequate written description should be withdrawn. The application clearly describes that peptides that "*bind to Aβ and are capable of blocking the fibril formation of Aβ-1-40 and are therefore potentially useful as drugs.*" All of the claimed peptides have been shown to bind Aβ-1-40 (see Figs. 2A and 2B) and the Examiner recognized (see page 3, 1st paragraph, of the final Office Action) that one tested compound was shown to inhibit polymerization. The value of the invention was also recognized by the scientific community, as those results were peer-reviewed and published in the prestigious *Journal of Biological Chemistry* (Tjernberg et al., J. Biol. Chem. 271(15):8545-8548, 1996; a copy is enclosed). Applicants thus submit that the application describes the use of peptides such as those specified in the present claims for the inhibition of amyloid β peptide polymerization. This rejection should therefore be withdrawn.

Applicants further request that, if possible, the prior Restriction Requirement in this case be reconsidered because, since the filing of the application, ownership of the application had changed and the present owners had only recently studied the application in detail, and had only then identified very specific material that they would like to claim. Further, the pending claims

were drafted with the cited prior art under close consideration, to enable straightforward and rapid prosecution. The pending claims fall within the elected restriction group, Group IV, and include sequences that encompass the elected species (KLVFF; His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-Glu and Val-His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala). Applicants respectfully request that the other sequences specified in the claims (His-Gln-Lys-Leu-Val-Phe, His-His-Gln-Lys-Leu-Val-Phe, Val-His-His-Gln-Lys-Leu-Val-Phe, Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe, and Gly-Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val) be examined in this application, upon a determination that claims specifying the elected species are allowable.

Applicants finally note that the Form PTO 1449 that was submitted with an Information Disclosure Statement filed on November 26, 2003 and returned in the Office Action February 15, 2006, has not been fully initialed. Specifically, Applicants respectfully request confirmation that the documents listed under the section 'Foreign Patent Documents' were considered, and that the Form PTO 1449 be initialed with respect to the foreign patent documents and returned to us.

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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